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USE OF TETANUS ALLERGEN FOR DETERMINING THE SENSITIVITY OF PEOPLE TO TETANUS ANATOXIN

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Foreign Technology Division
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Block	Italic	Transliteration	Block	Italic	Transliteration
А а	*А а*	A, a	Р р	*Р р*	R, r
Б б	*Б б*	B, b	С с	*С с*	S, s
В в	*В в*	V, v	Т т	*Т т*	T, t
Г г	*Г г*	G, g	У у	*У у*	U, u
Д д	*Д д*	D, d	Ф ф	*Ф ф*	F, f
Е е	*Е е*	Ye, ye; E, e*	Х х	*Х х*	Kh, kh
Ж ж	*Ж ж*	Zh, zh	Ц ц	*Ц ц*	Ts, ts
З з	*З з*	Z, z	Ч ч	*Ч ч*	Ch, ch
И и	*И и*	I, i	Ш ш	*Ш ш*	Sh, sh
Й й	*Й й*	Y, y	Щ щ	*Щ щ*	Shch, shch
К к	*К к*	K, k	Ъ ъ	*Ъ ъ*	"
Л л	*Л л*	L, l	Ы ы	*Ы ы*	Y, y
М м	*М м*	M, m	Ь ь	*Ь ь*	'
Н н	*Н н*	N, n	Э э	*Э э*	E, e
О о	*О о*	O, o	Ю ю	*Ю ю*	Yu, yu
П п	*П п*	P, p	Я я	*Я я*	Ya, ya

*ye initially, after vowels, and after ъ, ь; e elsewhere. When written as ё in Russian, transliterate as yë or ë. The use of diacritical marks is preferred, but such marks may be omitted when expediency dictates.

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GRAPHICS DISCLAIMER

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RUSSIAN AND ENGLISH TRIGONOMETRIC FUNCTIONS

Russian	English
sin	sin
cos	cos
tg	tan
ctg	cot
sec	sec
cosec	csc
sh	sinh
ch	cosh
th	tanh
cth	coth
sch	sech
csch	csch
arc sin	$\sin^{-1}$
arc cos	$\cos^{-1}$
arc tg	$\tan^{-1}$
arc ctg	$\cot^{-1}$
arc sec	$\sec^{-1}$
arc cosec	$\csc^{-1}$
arc sh	$\sinh^{-1}$
arc ch	$\cosh^{-1}$
arc th	$\tanh^{-1}$
arc cth	$\coth^{-1}$
arc sch	sech^{-1}
arc csch	csch^{-1}
rot	curl
lg	log

GREEK ALPHABET

Alpha	A	α	∝	Nu	N	ν	
Beta	B	β		Xi	Ξ	ξ	
Gamma	Γ	γ		Omicron	O	o	
Delta	Δ	δ		Pi	Π	π	
Epsilon	E	ε	∈	Rho	P	ρ	ϱ
Zeta	Z	ζ		Sigma	Σ	σ	ς
Eta	H	η		Tau	T	τ	
Theta	Θ	θ	$\$$	Upsilon	T	υ	
Iota	I	ι		Phi	Φ	φ	ϕ
Kappa	K	$\varkappa$	κ	Chi	X	χ	
Lambda	Λ	λ		Psi	Ψ	ψ	
Mu	M	μ		Omega	Ω	ω	

USE OF TETANUS ALLERGEN FOR DETERMINING THE SENSITIVITY OF PEOPLE TO TETANUS ANATOXIN

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State Control Institute imeni Tarasevich, Institute of Epidemiology and Microbiology imeni Gamaleya of the Academy of Medical Sciences, USSR and the Institute imeni Sklifosovskiy, Moscow (Received 17 August 1970).

Peacetime research on tetanus epidemiology in the USSR and in other countries (Matveyev, 1960; Chernaya and Kovtunovich, 1968; Bychenko, 1970) made it possible to arrive at the conclusion that in the majority of cases (50-80%) the traumas, which preceded a disease, were so insignificant that the victims did not appeal for medical assistance. This important fact attests to the fact that reliable protection from tetanus can be provided for only by means of the continuous immunization of the population. Special prophylaxis even with its 100% efficiency is capable of preventing the development of the disease in only $\frac{1}{5}$ part of the persons, who got traumas potentially dangerous with respect to tetanus. However, it continues to play important part in the solution of the problem concerning the protection of each wounded person against tetanus. The individual selection of remedies for the special prophylaxis of tetanus depends on a number of factors: 1) on information about vaccinations with tetanus anatoxin in the past,

2) the state of immunity to tetanus at the moment of examination (titer of antitoxin in the blood serum), 3) on the sensitivity to antitetanus serum or tetanus antitoxin (allergy).

Since the registration of vaccinations against tetanus in adults is still insufficiently imposed, the development of a rapid method of detection of the antitoxin in the blood serum and of tests to determine increased sensitivity to tetanus anatoxin and antitetanus serum has important practical value. The timely application of such methods and tests will make it possible, on one hand, to insure protection against tetanus, but on the other hand, to avoid the complications connected with the use of a serum or anatoxin in many cases.

The purpose of this work was research on the state of sensitivity to tetanus anatoxin in people by measuring the concentration of antitoxin in the blood serum with the aid of neutralization reactions and macro and microhemagglutination with the simultaneous determination of the sensitivity of the examined persons to the tetanus allergens.

Tetanus allergen was prepared for the first time by Shvarts and Shlyakhov according to the original method (1970). Two tetanus allergens in the present work are used, from concentrated purified tetanus anatoxin and from microbe cells of a 3-day culture of the No. 154 strain Cl tetani (MRTU-42, No. 344-69).

Observations were performed on 201 volunteers from 16 to 65 years of age (172 women and 29 men), 80% of whom were immunized in the past with tetanus anatoxin.

Blood from a vein in a 5-7 ml quantity was taken to determine the titer of antitoxin of each person. The titer of antitoxin was determined by three methods: in a neutralization reaction (RN) in white mice, in a passive hemagglutination (RPGA) reaction which was produced according to the previously described method (Bychenko and co-auth., 1969), and with the aid of an allergic test.

The allergen was administered intradermally to volunteers in the left forearm in a 0.1 ml quantity (30 µg of protein). This dose usually caused skin hyperemia of a diameter of more than 1 cm in persons, immunized with the tetanus anatoxin and who had antitoxin in a quantity equal or exceeding 0.1 ME/ml, in the blood serum.[1] The diameter of the hyperemia was measured 24 hours after the administration of the allergen.

For the reimmunization and immunization of the volunteers the tetanus adsorbed anatoxin of series No. 763 containing 20 EC in 1 ml was used. On the 10th day after each administration of anatoxin a skin sample was made and the titer of antitoxin in the blood was checked. The obtained results were subjected to statistical processing, utilizing correlation and regressing analyses.

Depending on the nature of the skin test with tetanus allergen and the antitoxin level in the blood serum, the examined persons consisted of four independent groups (Table 1). The 1st group included the persons whose skin reaction diameter exceeded 10 mm, and the titer of antitoxin in the blood serum exceeded 0.01 in 1 ml. The 2nd group included all the volunteers whose skin reaction to the allergen was negative, but the titer of antitoxin in the blood serum was below 0.001 in 1 ml. The third group consisted of those persons whose skin test was positive (diameter of the hyperemia $\geq$10 ml), but the titer of antitoxin in the blood serum was below 0.001 in 1 ml. Finally, the 4-th group had to consist of the volunteers whose skin reaction would be negative, but the titer of antitoxin in the blood serum would be above 0.01 in 1 ml. However, in the present investigation of such persons it did not appear.

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[1]ME - International Unit or Mass Unit; EC - Serum Unit: probable expansions.

Table 1. Distribution of volunteers by groups depending on the nature of the skin reaction and concentration of antitoxin in the blood.

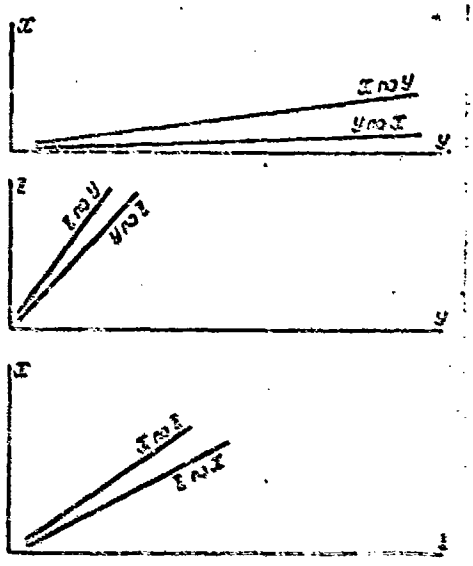
Number examined	Results of the investigation of the groups				Total
	1st	2d	3d	4th	
	+ / +	1 / 1	1 / +	+ / 1	
Men	19	4	6	0	29
Women	85	26	61	0	172
Total	104	30	67	0	201

Designations: +/+ presence of a skin reaction and antitoxin; -/- absence of a skin reaction and antitoxin; +/- presence of a skin reaction and absence of antitoxin; -/+ absence of a skin reaction and presence of antitoxin.

In 134 volunteers (67%) the agreement of the nature of the skin reaction with the detection of antitoxin in the blood was noted, i.e., both of these signs were either positive (1st group) or negative (2nd group). In the remaining 33% of the inspected persons the results of the determination of the indicated signs did not coincide.

Correlation analysis of the obtained results made it possible to establish that between the antitoxin level in the blood serum and the diameter of the skin reaction to the administration of the allergens there was a rectilinear connection. The correlation coefficients were equal to: 0.5[illegible] when using an allergen from anatoxin and [illegible].41 when using an allergen from microbe cells.

Despite the fact that the degree of this connection was not high, the reaction of the examined persons is indisputably specific. The fact that in 67% of the people an explicit dependence between the presence of antitoxin in the blood serum and the skin test results was observed attested to this. Furthermore, we were never able to fix a negative skin reaction to the allergen in those who had a detectable, with the aid of the neutralization reaction, quantity of antitoxin in the blood. The titer of antitoxin and skin reaction to the administration of the allergen changed relative to each other like the different signs (see figure).



Regression analysis of data, characterizing the connection between the skin reaction to allergens and titers of antitoxin in the blood of volunteers. X is the diameter (in mm) of the skin hyperemia on the site of the administration of the allergen, obtained from the anatoxin; U is the geometric titer of antitoxin (in ME/ml); Z is the diameter (in mm) of the skin hyperemia at the site of the administration of the allergen, obtained from cells Cl tetani.

Analogous results were obtained by Shvarts and Shlyakhov (1970).

The positive reaction to the allergens of people, in whose blood it was impossible to detect the antitoxin, was the most difficult to explain. In the past, this reaction could bear a traceable nature in vaccination with tetanus anatoxin. The answer to this question could be obtained only by administering a stimulating dose of anatoxin to volunteers. With this aim, 15 arbitrarily selected volunteers of the 3rd group were administered 20 EC of the adsorbed tetanus anatoxin. In 8 of them the build-up of the titer of antitoxin with the aid of the neutralization reaction was possible to determine on the 10th, and in 7, on the 40th

day after immunization (Table 2). In 11 examined persons (73.3%) the concentration of antitoxin in the blood exceeded considerably 0.01 ME/ml, which attested to the revaccinating action of the anatoxin.

Table 2. Change in titers of antitoxin in volunteers of the 3rd group after administration of the stimulating dose of anatoxin (20 EC).

No. p/p	Titer of antitoxin (in ME/ml) on the 10th day		No. p/p	Titer of antitoxin (in ME/ml) on the 40th day	
	RN*	RPGA**		RN*	RPGA**
1	7.5	256.0	1	0.75	0.25
2	7.5	128.0	2	0.75	1.0
3	3.0	64.0	3	0.75	0.5
4	0.75	64.0	4	0.75	0.31
5	0.01	0.03	5	0.5	0.125
6	0.3	256.0	6	0.006	0.003
7	0.006	0.016	7	0.06	0.03
8	0.006	0.016			

*RN, Neutralization Reaction; **RPGA, Passive hemagglutination reaction.

The volunteers of the 2nd group (15 people, who did not have detectable concentrations of antitoxin for proof of the specificity of the allergen action and who did not react to the allergens) obtained two injections of tetanus anatoxin (20 EC) with a 4-week interval in the blood. The content of antitoxin in the blood was checked and a skin test with allergens was made on the 10th day after each injection in these persons.

The skin test for allergens was positive in all the volunteers, whereas a noticeable build-up of the titer of antitoxin was noted in only 5 of them (Table 3) on the 10th day after the first injection of anatoxin. After the second stimulating dose of anatoxin the intensity of the allergic reaction in all those who

Table 3. Change in titers of antitoxin and intensity of the allergic reaction in volunteers of the 2nd group.

No. p/p	On the 10th day after the first administration of 20 EC of anatoxin				On the 10th day after the second administration of 20 EC of anatoxin			
	titer of antitoxin (in ME/ml)		diameter of hyperemia (in mm)		Titer of antitoxin (in ME/ml)		diameter of hyperemia (in mm)	
	RN	RPGA	allergen from the anatoxin	allergen from the cells	RN	RPGA	allergen from the anatoxin	allergen from the cells
1	0.01	0.125	15	20	0.75	0.5	15	25
2	0.01	0.007	10	20	0.75	0.25	15	20
3	0.01	0.03	10	30	0.1	0.25	30	50
4	0.3	1.0	15	30	0.5	2.0	20	40
5	1.5	4.0	30	45	3.0	16.0	30	40
6	0.0055	0.007	25	32	0.75	0.25	25	32
7	0.0055	0.03	15	20	0.75	20	10	25
8	<0.001	<0.001	20	3.5	3.5	1.0	27	40
9	<0.001	<0.001	50	70	0.75	0.25	10	27
10	<0.001	<0.001	25	35	0.75	0.25	25	45
11	<0.001	<0.001	20	32	0.75	0.5	12	30
12	<0.001	<0.001	35	50	7.5	128.0	35	55
13	<0.001	<0.001	5	10	0.055	0.03	15	35
14	<0.001	<0.001	10	15	0.75	4.0	20	35
15	<0.001	<0.001	25	35	0.75	4.0	30	35

were immunized remained at the previous level, whereas the concentration of antitoxin in the blood was noticeably increased. These results indicated the possibility of using an intradermal test with allergens for determining of the early immunological reaction of the human organism to tetanus anatoxin in that period when the concentration of antitoxin in the blood is still very low (<0.001 ME/ml). In this case the absence of the necessary direct dependence of the diameter of hyperemia at the site of the administration of the allergen on the value of the revealed titer of the antitoxin was noteworthy.

Conclusions

1. The specificity of the action of the tetanus allergens was exhibited in the fact that they always caused a local reaction (during intradermal administration) in people, who had detectable concentrations of the antitoxin ($\geq$0.001 ME/ml) in the blood.

2. Between the titers of the circulating antitoxin and the intensity of the skin reaction to the allergens in people slight linear dependence (correlation coefficients 0.55 and 0.41) is noted, which attests to the nonidentity of both tests.

3. The simultaneous use of the rapid method of detection of the antitoxin in the blood (passive hemagglutination reaction) and the intradermal test with allergens made it possible to establish that 50% of those examined (104 of the 201) with an unknown inoculative anamnesis obtained the tetanus anatoxin in the past.

4. The intradermal test with tetanus allergens can be important for revealing persons with increased sensitivity to tetanus anatoxin and selecting the remedies for the prophylaxis of tetanus in wounded persons with unknown inoculative anamnesis.

BIBLIOGRAPHY

Быченко Б. Д., Матвеев К. М., Строганова М. К. и др. Материалы научной конференции Государств. контрольного ин-та медицинских биологических препаратов им. Л. А. Тарасевича. М., 1969, с. 91. — Матвеев К. И. Эпидемиология и профилактика столбняка. М., 1960. — Черная Л. А. и Ковтунович Г. П. Столбняк. М., 1968. — Шварц С. А., Шляхов Э. Н. Материалы Всесоюзной межинститутской конференции, посвященной 125-летию со дня рождения И. И. Мечникова. М., 1970.

The authors discuss the problem of a possibility of using tetanus allergen for detection of increased sensitivity of man to tetanus toxoid. Two allergens (obtained by the method of Runova) — the first from the toxoid, and the second from the microbial cells, were investigated. In parallel with intradermal tests, a determination was male of the titre of the antitoxin circulating in the blood.

It was shown that the action of the allergens was specific — a local reaction in the form of hyperemia always appeared in persons whose blood antitoxin level was $\geq$0,001 IU/ml.

Intradermal test with allergens has offered a possibility of detecting an early immunological reaction of the organism in response to the administration of tetanus toxoid, i. e. before the antitoxin appeared in the blood of the immunized persons. Intradermal test with an allergen could be used as an auxiliary test to passive hemagglutination reaction to determine the state of increased sensitivity of man to tetanus toxoid.